Targeted Nutrition Therapy
Nutrition Masters Course

Nilima Desai, MPH, RD
Learning Objectives

• Review clinical studies on innovative, targeted nutrition therapies for:
  o Blood glucose management
  o Dyslipidemia
  o Gastrointestinal health
Randomized Controlled Trials at Joslin Diabetes Center for Blood Glucose Management

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• Rigorous, head-to-head comparison of nutrition therapy (NT) methods
• 108 patients (62 female, 46 male; 18-80 years old) with type 2 diabetes (T2D)
• Baseline characteristic (averages):
  o Age: 60, Weight: 101.4 kg, BMI: 35.2, HbA1c: 8.07%
• Patients randomized to 1 of 3 NT lifestyle interventions, for 16 weeks:
  o Group A: Met with RD for individualized dietary plan
  o Group B: Met with RD and followed structured dietary plan, including diabetes-specific nutrition formula (meal replacement)
  o Group C: Same as Group B + increased patient-RD interactions
Joslin Study #1: Results
Changes in HbA1c and Body Weight over 16 Weeks

Figure 3. Change in HbA₁c Over 16 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 16</th>
<th>Baseline</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA₁c (%)</td>
<td>8.19</td>
<td>8.22</td>
<td>7.91</td>
<td>7.28</td>
</tr>
</tbody>
</table>

Mean HbA₁c reduction
-0.64±0.13%

Mean Weight reduction
-3.0±0.6 kg or 3.0±0.6%

Values are mean ± SEM. Individualized Dietary Group (n=33), Structured Dietary Group (n=48)


Figure 4. Change in body weight Over 16 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>100</td>
<td>90</td>
</tr>
</tbody>
</table>

p<0.01

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Statistically significant results:
- All 3 groups experienced ↓ in energy intake, total carbs, total fat, and saturated fat
- ↓ Body weight, ↓ % body fat, and ↓ waist circumference in Groups B and C
- ↓ Visceral fat levels in Group B only
- Significant ↓ in HbA1c for Groups B and C

Conclusions:
- RDs play a critical role in partnering with patients with T2D to develop and implement NT interventions
- Structured NT (Groups B and C) were superior to individualized eating plan (Group A) in helping patients improve glycemic control and CVD risk factors
- The diabetes-specific nutrition formula (meal replacement) was an important, differentiating feature of the structured meal plan approach (Groups B and C) and success

Joslin Study #2: Three-Way, Cross-Over Clinical Study

**Study Objective:**

Compare the post-prandial glycemic response to a single serving of 2 nutritional formulas (novel vs. standard) vs. oatmeal breakfast of equal calories in patients with type 2 diabetes.

**Open-label, 3-way, cross-over randomized study conducted at the Joslin Diabetes Center**

- Subjects enrolled in this study came for 3 visits on 3 separate days. All 3 visits had to be completed in a 3-week period with at least 2 days between each visit.
- On each visit, subjects were fasting overnight and then served a food product with a caloric value of 200 kcal.
- The food product consumed was either a novel nutritional formula, standard nutritional formula, or regular oatmeal.

**Patients with type 2 diabetes**

(N=22)

Diabetes duration (yrs): 9.5 ± 9.8

Visit 1

Patient consumed: 1 serving/day 200 kcal

Visit 2

Patient consumed: 1 serving/day 200 kcal

Week 3

Patient consumed: 1 serving/day 200 kcal


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A novel nutritional formula resulted in a more pronounced secretion of insulin, resulting in a more sustained and balanced glucose response curve.

Joslin Study #2: GLP-1 Results

The novel nutritional formula resulted in a more pronounced secretion of glucagon-like peptide-1 (GLP-1), resulting in a more sustained and balanced glucose response curve.

What is GLP-1?

• Glucagon-like peptide-1 (GLP-1) is a gut-derived peptide secreted from intestinal L-cells and is released in response to food consumption

• Main action - stimulates insulin secretion and inhibits glucagon secretion, thereby promoting postprandial glucose homeostasis

• Slows gastric emptying and induces satiety

Summary of Joslin Study Findings with Targeted NT for T2D

- Reductions in weight, body fat, waist circumference, and HbA1c
- Improvements in diet quality; reduction in energy intake
- More pronounced GLP-1 production, which can help regulate appetite and post-prandial glucose levels
- A more sustained and balanced glucose control without a hypoglycemic effect

Summary of Study Findings with NT in T2D

- Previous studies have shown that intensive diet and lifestyle interventions have resulted in delaying the onset of diabetes by 58% compared to placebo, statistically significant reductions in HbA1c, fasting plasma glucose, CVD risk factors, and weight loss¹.

- In clinical practice, combining an innovative nutritional formula with dietary and lifestyle recommendations may provide clinical benefit. This combination can form an important part of a medical nutrition therapy program for blood glucose management.

Practice-Based Research with Innovative Nutritional Formula for Dyslipidemia

IRB-approved, open-label, case observation series
Received 2 servings of innovative nutritional formula/day for 8 Weeks

AT EACH TIME-POINT:
Assessment of Plasma Lipids, Body Weight, Metabolic Syndrome Criteria, Diet and Lifestyle Factors

Enrolled patients with dyslipidemia
- Total Cholesterol >220 mg/dL
- LDL cholesterol >155 mg/dL

September 2015

December 2015

IRB-approval of protocol and sites

Baseline

Week 4

Week 8


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Enrolled
n=24

1 pea/rice lost to f/u
2 soy lost to f/u

Week 4
n=21

3 pea/rice lost to f/u
6 soy lost to f/u

Week 8
n=12

Analysis Plan
Differences from baseline at 4 weeks and 8 weeks assessed by paired t-test
Mean data presented on following slides calculated for completers of that variable

Pea/Rice (n)  Soy (n)
13        11

Pea/Rice (n)  Soy (n)
12         9

Pea/Rice (n)  Soy (n)
9          3
Total Cholesterol
Significantly Reduced at 4 Weeks

- Group moved from high down to borderline high total cholesterol
- 47% of subjects re-classified into a lower TC risk category
- Up to 27.6% reduction at 4 weeks
- No significant difference between soy and pea group

* denotes p-value = 0.01, as assessed by paired t-tests between baseline and 4-week data


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LDL Cholesterol
Significantly Reduced at 4 Weeks

15pt reduction (-8.5%)

• Group moved from high down to borderline high LDL in 4 weeks
• 56% of subjects re-classified into a lower LDL cholesterol risk category
• Up to 35.9% reduction at 4 weeks
• No significant difference between soy and pea group

* denotes p-value = 0.01, as assessed by paired t-tests between baseline and 4-week data
Other Atherogenic Lipid Biomarkers Significantly Reduced Within 4 Weeks

- **Apo-B (mg/dL)**
  - Baseline: 140 (n=7)
  - Week 4: 128* (n=7)
  - 8.2% reduction within 4 weeks

- **Non-HDL-C (mg/dL)**
  - Baseline: 126 (n=12)
  - Week 4: 118* (n=12)
  - 8.6% reduction within 4 weeks

* denotes p-value < 0.05, as assessed by paired t-tests between baseline and 4-week data

Reproduced with permission from: Stagg, J, Change, N, Whole Health Chicago
Practice-Based Research Results with UMC Medical Food: Effects on Plasma Lipid Profile and Selected Clinical Biomarkers for Metabolic Syndrome, Sept-December 2015.

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# Metabolic Syndrome Criteria

**Improvement Noted at 4 Weeks**

$n=21$

<table>
<thead>
<tr>
<th></th>
<th>Waist (inches)</th>
<th>SBP (mmHg)</th>
<th>HDL-C (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ref. range</strong></td>
<td>&lt;40/35 (M/F)</td>
<td>&lt;135</td>
<td>&lt;40/50 (M/F)</td>
<td>&lt;150</td>
<td>&lt;100</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>40.5</td>
<td>125.8</td>
<td>60.0</td>
<td>144.7</td>
<td>95.7</td>
</tr>
<tr>
<td><strong>4 Weeks</strong></td>
<td>39.7</td>
<td>117.7</td>
<td>60.5</td>
<td>136.0</td>
<td>96.8</td>
</tr>
</tbody>
</table>

- 1 in.
- 6%

4% reduction in CVD risk

12.8% reduced CVD risk

No clinical change

Remained WNL

* Significant reduction (p<0.05) from baseline as assessed by paired t-tests between time-points

Continued Reduction
LDL Cholesterol in Group that Completed 8 Weeks

- Up to 21% reduction
- 67% of subjects re-classified to lower risk category
- 6.4% reduction in total cholesterol (up to 16% reduction)
- No further improvements in other metabolic syndrome criteria

<table>
<thead>
<tr>
<th>LDL-C Change (mg/dL)‡</th>
<th>n=24</th>
<th>n=12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>145</td>
<td></td>
</tr>
</tbody>
</table>

‡ mean data from sub-group completing 8-week time-point only


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Study summary and conclusions

• Significant reductions in the atherogenic lipid profile (LDL-C, apoB, non-HDL cholesterol), and risk reclassification into lower risk group
• Improvements in particle size in select cases where measured
• Improvements in metabolic syndrome-related variables seen, and waist circumference and systolic blood pressure reductions at a magnitude previously associated with a lowering of CVD risk\(^1,2\)


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Study summary and conclusions

• Previous studies have shown that intensive diet and lifestyle interventions have resulted in LDL lowering benefits of 10.8% in 8 weeks, with an added benefit of a nutritional formula of 8.1% in these studies.\(^1\) This study showed a 10% reduction in LDL cholesterol in 8 weeks, with additional positive changes in atherogenic lipid profile and cardiometabolic risk biomarkers within 4 weeks.

• In clinical practice, an additional emphasis on combining an innovative nutritional formula with dietary and lifestyle recommendations can bring broad benefit. This combination can form the basis of a medical nutrition therapy program for longer-term management of dyslipidemia.

Practice-Based Research with Innovative Nutritional Formula for Gastrointestinal (GI) Function

*Single Arm, Open-Label Study*
Clinical Study Design

12 Patients with Gut Dysfunction

Ulcerative colitis (UC), Crohn's disease, Irritable Bowel Syndrome (IBS), or Celiac Disease

Took 2 servings/day of innovative nutritional formula for 6 weeks

Baseline

• Gastrointestinal Quality of Life Index (GIQLI) Questionnaire
• Study Product Dispensed
• Collect Stool at Home

Week 3 mid-study visit to confirm protocol compliance

Week 6

• Collect Stool at Home
• Gastrointestinal Quality of Life Index (GIQLI) Questionnaire
• Unused Study Product Returned

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Stagg J. Whole Health Associates, LLC, Avon, CT
Holder K. Center for Preventative Medicine, South Orange, NJ
Rice C. Forney Wellness, Forney, TX

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### Results

<table>
<thead>
<tr>
<th>GIQLI</th>
<th>Score Range</th>
<th>Results (Mean)</th>
<th>% Change</th>
<th>P-value (Paired T-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Score</strong></td>
<td>0-144</td>
<td>Baseline: 94.5 +/- 25.5</td>
<td>+ 20.8%</td>
<td>0.020</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Study End: 109.4 +/- 19.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GI Symptoms Domain</strong></td>
<td>0-76</td>
<td>Baseline: 53.3 +/- 10.3</td>
<td>+ 18.1%</td>
<td>0.022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Study End: 61.4 +/- 7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Social Function Domain</strong></td>
<td>0-16</td>
<td>Baseline: 10.7 +/- 3.8</td>
<td>+ 18.4%</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Study End: 12.3 +/- 3.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Total score, GI symptom domain, and Social function domain scores improved
- Higher scores are consistent with better quality of life
- Additional domain (physical function and emotional function) scores were improved, but did not reach statistical significance

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Results: Significantly Increased Bifidobacterium

<table>
<thead>
<tr>
<th>Bifidobacterium spp.</th>
<th>Reference Range</th>
<th>Results (mean +/- SD)</th>
<th>Mean % Change</th>
<th>p Value (Paired t-test)</th>
</tr>
</thead>
</table>
| ≤6.4E9               | Baseline: 1.2E9 +/- 1.5E9  
6 Weeks: 5.4E9 +/- 5.1E9 | +1890.1%  
(19-fold increase) | 0.026 |

2’-FL and IMO are key nutritional bioactives that are likely responsible for the increases in butyrate, SCFAs, and *Bifidobacterium* levels.
## Results: Significantly Enhanced Production of SCFAs Including Butyrate

<table>
<thead>
<tr>
<th></th>
<th>Reference Range</th>
<th>Results (mean +/- SD)</th>
<th>Mean % Change</th>
<th>P-value (Paired T-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n-Butyrate Concentration</strong></td>
<td>≥ 3.6 micromol/g</td>
<td>Baseline: 8.1 +/- 4.8  6 Weeks: 16.7 +/- 9.6</td>
<td>+ 594.0 %</td>
<td>0.040</td>
</tr>
<tr>
<td><strong>SCFA (Total)</strong></td>
<td>≥ 23.3 micromol/g</td>
<td>Baseline: 46.3 +/- 13.3 6 Weeks: 76.4 +/- 37.0</td>
<td>+ 72.2 %</td>
<td>0.026</td>
</tr>
</tbody>
</table>

(Total SCFAs = Butyrate + Acetate + Propionate)

- Levels of bacterial strains known to produce butyrate also increased
  - *F. prausnitzii* levels increased 20-fold (p=0.029)
  - *Roseburia* spp. levels increased 13-fold (p=0.091, non-significant)
- The increased production of butyrate in the gut is a potential mechanism for the reduction in GI symptoms demonstrated in this study

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Study Summary

GI symptoms and quality of life scores improved significantly

Significantly increased *Bifidobacterium* (19-fold)

Significantly enhanced production of SCFAs, including butyrate by 594.0% (on average)

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